



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁷ : C12N 15/63, A61K 48/00, 39/21, 48/00, C07K 14/00</p>	<p>A1</p>	<p>(11) International Publication Number: WO 00/14257</p> <p>(43) International Publication Date: 16 March 2000 (16.03.00)</p>
<p>(21) International Application Number: PCT/US99/20349</p> <p>(22) International Filing Date: 3 September 1999 (03.09.99)</p> <p>(30) Priority Data: 60/099,138 4 September 1998 (04.09.98) US</p> <p>(71) Applicant (for all designated States except US): SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH [US/US]; 1275 York Avenue, New York, NY 10021 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): SADELAIN, Michel [CA/US]; 401 E 89th Street #9K, New York, NY 10128 (US). BANDER, Neil, H. [US/US]; 2 Hemlock Hill, Chappaqua, NY 10128 (US). GONG, Michael [US/US]; 1233 York Avenue #15N, New York, NY 10021 (US).</p> <p>(74) Agent: LARSON, Marina, T.; Oppedahl & Larson LLP, P.O. Box 5270, Frisco, CO 80443-5270 (US).</p>		<p>(81) Designated States: CA, JP, US, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</p> <p>Published</p> <p><i>With international search report.</i></p> <p><i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>

(54) Title: FUSION RECEPTORS SPECIFIC FOR PROSTATE-SPECIFIC MEMBRANE ANTIGEN AND USES THEREOF

(57) Abstract

A fusion receptor composition which is effective to promote a cellular immune response to prostate-specific membrane antigen (PSMA) *in vivo* when the fusion receptors is expressed by T lymphocytes has the structure: PSMA-scFv: connector: cytoplasmic domain. The PSMA-scFv in this structure is a single chain antibody cloned from the V region genes of a hybridoma specific for PSMA. The connector region is provided to give a spacing between the OSMA-scFv and the cytoplasmic domain, such that both can retain substantial function. A suitable connector is the CD8 hinge, although other connectors of greater or lesser length might be used. The cytoplasmic domain is included to direct the function of the fusion receptor. One exemplary cytoplasmic domain which can be used in the fusion receptor of the invention is a T cell receptor ζ -chain cytoplasmic domain. An expression vector encoding the fusion receptor is transduced into primary T lymphocytes obtained from an individual to be treated. The transduced lymphocytes are returned to the patient where cells expressing the fusion receptor secrete interleukin 2 and proliferate in response to PSMA-positive cells. The resulting cytotoxic lymphocytes specifically lyse cells expressing PSMA and thus can be used to target PSMA-positive tumor cells and neovasculature.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						